

CLAIMS

We Claim:

1. A method for determining the sequence of a nucleic acid molecule, comprising:

(a) generating tagged nucleic acid fragments which are complementary to a selected target nucleic acid molecule, wherein a tag is correlative with a particular nucleotide and detectable by non-fluorescent spectrometry or potentiometry;
(b) separating the tagged fragments by sequential length;
(c) cleaving the tags from the tagged fragments; and
(d) detecting the tags by non-fluorescent spectrometry or potentiometry, and therefrom determining the sequence of the nucleic acid molecule.

2. The method according to claim 1 wherein the detection of the tags is by mass spectrometry, infrared spectrometry, ultraviolet spectrometry or potentiostatic amperometry.

3. The method according to claims 1 or 2 wherein the tagged fragments are separated in step (b) by a method selected from gel electrophoresis, capillary electrophoresis, micro-channel electrophoresis and HPLC.

4. The method according to claims 1 or 2 wherein the tagged fragments are cleaved in step (c) by a method selected from oxidation, reduction, acid-labile, base-labile, enzymatic, electrochemical, thermal, thiol exchange and photolabile methods.

5. The method according to claim 2 wherein the tags are detected by time-of-flight mass spectrometry, quadrupole mass spectrometry, magnetic sector mass spectrometry or electric sector mass spectrometry.

6. The method according to claim 2 wherein the tags are detected by coulometric detectors or amperometric detectors.
7. The method according to claims 1 or 2 wherein the tagged nucleic acid fragments are generated in step (a) from a 5' terminus to a 3' terminus.
8. The method according to claims 1 or 2 wherein step (a) generates more than four of the tagged nucleic acid fragments and each tag is unique for a nucleic acid fragment.
9. The method according to claims 1 or 2 wherein steps (b), (c) and (d) are performed in a continuous manner.
10. The method according to claims 1 or 2 wherein steps (b), (c) and (d) are performed in a continuous manner on a system.
11. The method according to claims 1 or 2 wherein one or more of the steps is automated.
12. The method according to claims 1 or 2 wherein the tagged fragments are generated from oligonucleotide primers that are conjugated to a tag at other than the 3' end of the primer.
13. The method according to claims 1 or 2 wherein the tagged fragments are generated from tagged dideoxynucleotide terminators.
14. The method according to claims 1 or 2 wherein at least one tagged nucleic acid fragment is a compound according to any one of claims 15 to 33.
15. A compound of the formula:

T^{ms} -L-X

wherein,

T^{ms} is an organic group detectable by mass spectrometry, comprising carbon, at least one of hydrogen and fluoride, and optional atoms selected from oxygen, nitrogen, sulfur, phosphorus and iodine;

L is an organic group which allows a T^{ms} -containing moiety to be cleaved from the remainder of the compound, wherein the T^{ms} -containing moiety comprises a functional group which supports a single ionized charge state when the compound is subjected to mass spectrometry and is selected from tertiary amine, quaternary amine and organic acid;

X is a functional group selected from hydroxyl, amino, thiol, carboxylic acid, haloalkyl, and derivatives thereof which either activate or inhibit the activity of the group toward coupling with other moieties, or is a nucleic acid fragment attached to L at other than the 3' end of the nucleic acid fragment;

with the provisos that the compound is not bonded to a solid support through X nor has a mass of less than 250 daltons.

16. A compound according to claim 15 wherein T^{ms} has a mass of from 15 to 10,000 daltons and a molecular formula of $C_{1-500}N_{0-100}O_{0-100}S_{0-10}P_{0-10}H_{\alpha}F_{\beta}I_{\delta}$ wherein the sum of α , β and δ is sufficient to satisfy the otherwise unsatisfied valencies of the C, N, O, P and S atoms.

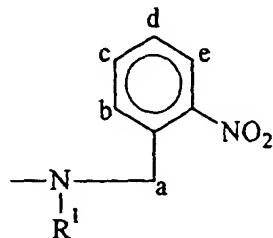
17. A compound according to claim 15 wherein T^{ms} and L are bonded together through a functional group selected from amide, ester, ether, amine, sulfide, thioester, disulfide, thioether, urea, thiourea, carbamate, thiocarbamate, Schiff base, reduced Schiff base, imine, oxime, hydrazone, phosphate, phosphonate, phosphoramidate, phosphonamide, sulfonate, sulfonamide or carbon-carbon bond.

18. A compound according to claim 17 wherein the functional group is selected from amide, ester, amine, urea and carbamate.

19. A compound according to claim 15 wherein L is selected from L^{hv} , L^{acid} , L^{base} , $L^{[O]}$, $L^{[R]}$, L^{enz} , L^{elec} , L^A and L^S , where actinic radiation, acid, base, oxidation, reduction, enzyme, electrochemical, thermal and thiol exchange, respectively, cause the T^{ms} -containing moiety to be cleaved from the remainder of the molecule.

20. A compound according to claim 19 wherein L^{hv} has the formula $L^1-L^2-L^3$, wherein L^2 is a molecular fragment that absorbs actinic radiation to promote the cleavage of T^{ms} from X, and L^1 and L^3 are independently a direct bond or an organic moiety, where L^1 separates L^2 from T^{ms} and L^3 separates L^2 from X, and neither L^1 nor L^3 undergo bond cleavage when L^2 absorbs the actinic radiation.

21. A compound according to claim 20 wherein $-L^2-L^3$ has the formula:



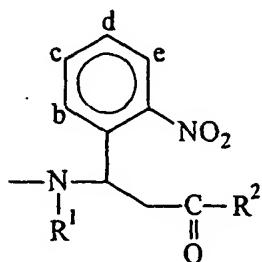
with one carbon atom at positions a, b, c, d or e being substituted with $-L^3-X$ and optionally one or more of positions b, c, d or e being substituted with alkyl, alkoxy, fluoride, chloride, hydroxyl, carboxylate or amide; and R^1 is hydrogen or hydrocarbyl.

22. A compound according to claim 21 wherein X is $\text{---C}(\text{---R}^2)\text{---}$ and R^2 is -

OH or a group that either protects or activates a carboxylic acid for coupling with another moiety.

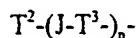
23. A compound according to claim 20 wherein L^3 is selected from a direct bond, a hydrocarbylene, $-\text{O}-\text{hydrocarbylene}$, and hydrocarbylene-($\text{O}-\text{hydrocarbylene}$) $_n\text{-H}$, and n is an integer ranging from 1 to 10.

24. A compound according to claim 15 wherein -L-X has the formula:



wherein one or more of positions b, c, d or e is substituted with hydrogen, alkyl, alkoxy, fluoride, chloride, hydroxyl, carboxylate or amide; and R¹ is hydrogen or hydrocarbyl.

25. A compound according to claim 15 wherein T^{m_s} has the formula:



T² is an organic moiety formed from carbon and one or more of hydrogen, fluoride, iodide, oxygen, nitrogen, sulfur and phosphorus, having a mass of 15 to 500 daltons;

T³ is an organic moiety formed from carbon and one or more of hydrogen, fluoride, iodide, oxygen, nitrogen, sulfur and phosphorus, having a mass of 50 to 1000 daltons;

J is a direct bond or a functional group selected from amide, ester, amine, sulfide, ether, thioester, disulfide, thioether, urea, thiourea, carbamate, thiocarbamate, Schiff base, reduced Schiff base, imine, oxime, hydrazone, phosphate, phosphonate, phosphoramido, phosphonamido, sulfonate, sulfonamide or carbon-carbon bond; and

n is an integer ranging from 1 to 50, and when n is greater than 1, each T³ and J is independently selected.

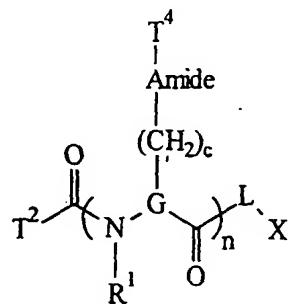
26. A compound according to claim 25 wherein T² is selected from hydrocarbyl, hydrocarbyl-O-hydrocarbylene, hydrocarbyl-S-hydrocarbylene, hydrocarbyl-

NH-hydrocarbylene, hydrocarbyl-amide-hydrocarbylene, N-(hydrocarbyl)hydrocarbylene, N,N-di(hydrocarbyl)hydrocarbylene, hydrocarbylacyl-hydrocarbylene, heterocyclhydrocarbyl wherein the heteroatom(s) are selected from oxygen, nitrogen, sulfur and phosphorus, substituted heterocyclhydrocarbyl wherein the heteroatom(s) are selected from oxygen, nitrogen, sulfur and phosphorus and the substituents are selected from hydrocarbyl, hydrocarbyl-O-hydrocarbylene, hydrocarbyl-NH-hydrocarbylene, hydrocarbyl-S-hydrocarbylene, N-(hydrocarbyl)hydrocarbylene, N,N-di(hydrocarbyl)hydrocarbylene and hydrocarbylacyl-hydrocarbylene, as well as derivatives of any of the foregoing wherein one or more hydrogens is replaced with an equal number of fluorides.

27. A compound according to claim 25 wherein T³ has the formula -G(R²)-, G is C₁₋₆ alkylene having a single R² substituent, and R² is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl-fused cycloalkyl, cycloalkenyl, aryl, aralkyl, aryl-substituted alkenyl or alkynyl, cycloalkyl-substituted alkyl, cycloalkenyl-substituted cycloalkyl, biaryl, alkoxy, alkenoxy, alkynoxy, aralkoxy, aryl-substituted alkenoxy or alkynoxy, alkylamino, alkenylamino or alkynylamino, aryl-substituted alkylamino, aryl-substituted alkenylamino or alkynylamino, aryloxy, arylamino, N-alkylurea-substituted alkyl, N-arylurea-substituted alkyl, alkylcarbonylamino-substituted alkyl, aminocarbonyl-substituted alkyl, heterocycl, heterocycl-substituted alkyl, heterocycl-substituted amino, carboxyalkyl substituted aralkyl, oxocarbocycl-fused aryl and heterocyclalkyl; cycloalkenyl, aryl-substituted alkyl and, aralkyl, hydroxy-substituted alkyl, alkoxy-substituted alkyl, aralkoxy-substituted alkyl, alkoxy-substituted alkyl, aralkoxy-substituted alkyl, amino-substituted alkyl, (aryl-substituted alkyloxycarbonylamino)-substituted alkyl, thiol-substituted alkyl, alkylsulfonyl-substituted alkyl, (hydroxy-substituted alkylthio)-substituted alkyl, thioalkoxy-substituted alkyl, hydrocarbylacylamino-substituted alkyl, heterocyclacylamino-substituted alkyl, hydrocarbyl-substituted-heterocyclacylamino-substituted alkyl, alkylsulfonylamino-substituted alkyl, arylsulfonylamino-substituted alkyl, morpholino-alkyl, thiomorpholino-alkyl, morpholino carbonyl-substituted alkyl, thiomorpholinocarbonyl-substituted alkyl, [N-(alkyl, alkenyl or alkynyl)- or N,N-[dialkyl, dialkenyl, dialkynyl or (alkyl, alkenyl)-amino]carbonyl-substituted alkyl, heterocyclaminocarbonyl,

heterocylylalkyleneaminocarbonyl, heterocylylaminocarbonyl-substituted alkyl, heterocylylalkyleneaminocarbonyl-substituted alkyl, N,N-[dialkyl]alkyleneaminocarbonyl, N,N-[dialkyl]alkyleneaminocarbonyl-substituted alkyl, alkyl-substituted heterocylylcarbonyl, alkyl-substituted heterocylylcarbonyl-alkyl, carboxyl-substituted alkyl, dialkylamino-substituted acylaminoalkyl and amino acid side chains selected from arginine, asparagine, glutamine, S-methyl cysteine, methionine and corresponding sulfoxide and sulfone derivatives thereof, glycine, leucine, isoleucine, allo-isoleucine, tert-leucine, norleucine, phenylalanine, tyrosine, tryptophan, proline, alanine, ornithine, histidine, glutamine, valine, threonine, serine, aspartic acid, beta-cyanoalanine, and allo-threonine; alynyl, heterocylylcarbonyl, aminocarbonyl, amido, mono- or dialkylaminocarbonyl, mono- or diarylaminocarbonyl, alkylarylamino, diarylaminocarbonyl, mono- or diacylaminocarbonyl, aromatic or aliphatic acyl, alkyl optionally substituted by substituents selected from amino, carboxy, hydroxy, mercapto, mono- or dialkylamino, mono- or diarylamino, alkylarylamino, diarylmino, mono- or diacylamino, alkoxy, alkenoxy, aryloxy, thioalkoxy, thioalkenoxy, thioalkynoxy, thioaryloxy and heterocylyl.

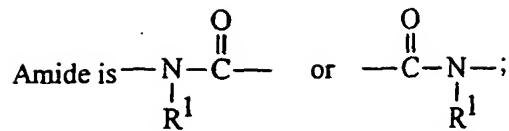
28. A compound according to claim 25 having the formula:



wherein

G is $(CH_2)_{1-6}$ wherein a hydrogen on one and only one of the CH_2 groups of each G is replaced with- $(CH_2)_c$ -Amide- T^4 ;

T^2 and T^4 are organic moieties of the formula $C_{1-25}N_{0-9}O_{0-9}S_{0-3}P_{0-3}H_\alpha F_\beta I_\delta$ wherein the sum of α , β and δ is sufficient to satisfy the otherwise unsatisfied valencies of the C, N, O, S and P atoms;



R^1 is hydrogen or C_{1-10} alkyl;

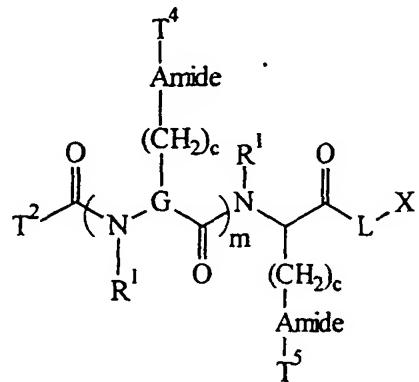
c is an integer ranging from 0 to 4;

X is defined according to claim 1; and

n is an integer ranging from 1 to 50 such that when n is greater than 1, G , c ,

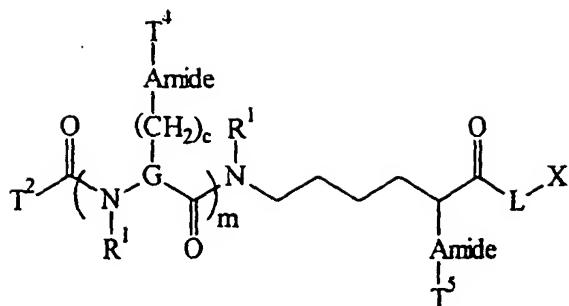
Amide, R^1 and T^4 are independently selected.

29. A compound according to claim 28 having the formula:



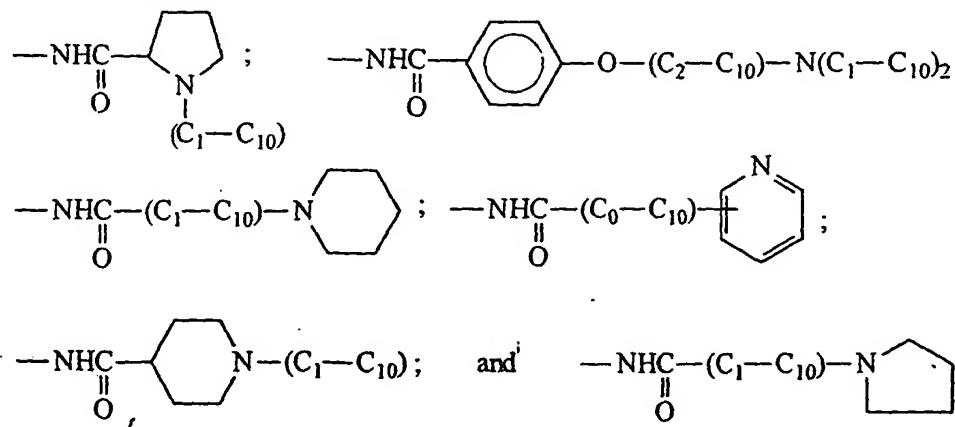
wherein T^5 is an organic moiety of the formula $\text{C}_{1-25}\text{N}_{0-9}\text{O}_{0-9}\text{S}_{0-3}\text{P}_{0-3}\text{H}_{\alpha}\text{F}_{\beta}\text{I}_{\delta}$ wherein the sum of α , β and δ is sufficient to satisfy the otherwise unsatisfied valencies of the C, N, O, S and P atoms; and T^5 includes a tertiary or quaternary amine or an organic acid; and m is an integer ranging from 0-49.

30. A compound according to claim 28 having the formula:

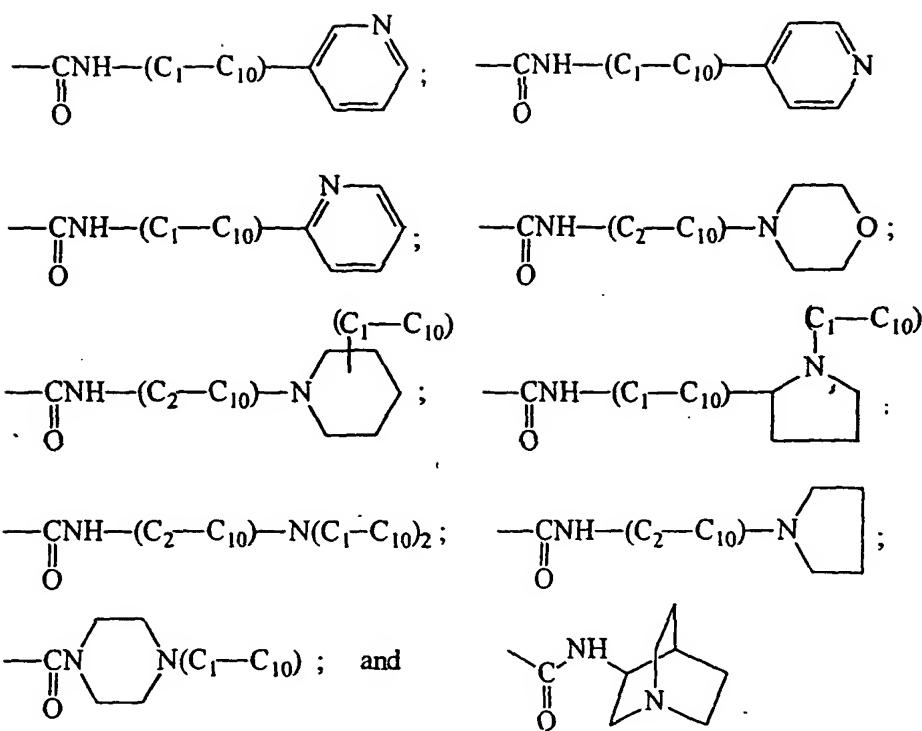


wherein T^5 is an organic moiety of the formula $C_{1-25}N_{0-9}O_{0-9}S_{0-3}P_{0-3}H_aF_\beta I_\delta$ wherein the sum of α , β and δ is sufficient to satisfy the otherwise unsatisfied valencies of the C, N, O, S and P atoms; and T^5 includes a tertiary or quaternary amine or an organic acid; and m is an integer ranging from 0-49.

31. A compound according to any one of claims 29 and 30 wherein -Amide- T^5 is selected from:



32. A compound according to any of claims 29 and 30 wherein -Amide- T^5 is selected from:



33. A compound according to any one of claims 25-29 wherein T^2 has the structure which results when one of the following organic acids is condensed with an amine group to form $\text{T}^2\text{-C(=O)-N(R}^1\text{)}$: Formic acid, Acetic acid, Propiolic acid, Propionic acid, Fluoroacetic acid, 2-Butynoic acid, Cyclopropanecarboxylic acid, Butyric acid, Methoxyacetic acid, Difluoroacetic acid, 4-Pentylic acid, Cyclobutanecarboxylic acid, 3,3-Dimethylacrylic acid, Valeric acid, N,N-Dimethylglycine, N-Formyl-Gly-OH, Ethoxyacetic acid, (Methylthio)acetic acid, Pyrrole-2-carboxylic acid, 3-Furoic acid, Isoxazole-5-carboxylic acid, trans-3-Hexenoic acid, Trifluoroacetic acid, Hexanoic acid, Ac-Gly-OH, 2-Hydroxy-2-methylbutyric acid, Benzoic acid, Nicotinic acid, 2-Pyrazinecarboxylic acid, 1-Methyl-2-pyrrolecarboxylic acid, 2-Cyclopentene-1-acetic acid, Cyclopentylacetic acid, (S)-()-2-Pyrrolidone-5-carboxylic acid, N-Methyl-L-proline, Heptanoic acid, Ac-b-Ala-OH, 2-Ethyl-2-hydroxybutyric acid, 2-(2-Methoxyethoxy)acetic acid, p-Toluic acid, 6-Methylnicotinic acid, 5-Methyl-2-pyrazinecarboxylic acid, 2,5-Dimethylpyrrole-3-carboxylic acid, 4-Fluorobenzoic acid, 3,5-Dimethylisoxazole-4-carboxylic acid, 3-Cyclopentylpropionic acid, Octanoic acid, N,N-Dimethylsuccinamic acid, Phenylpropionic acid, Cinnamic acid, 4-Ethylbenzoic acid, p-Anisic acid, 1,2,5-Trimethylpyrrole-3-carboxylic

acid, 3-Fluoro-4-methylbenzoic acid, Ac-DL-Propargylglycine, 3-(Trifluoromethyl)butyric acid, 1-Piperidinopropionic acid, N-Acetylproline, 3,5-Difluorobenzoic acid, Ac-L-Val-OH, Indole-2-carboxylic acid, 2-Benzofurancarboxylic acid, Benzotriazole-5-carboxylic acid, 4-n-Propylbenzoic acid, 3-Dimethylaminobenzoic acid, 4-Ethoxybenzoic acid, 4-(Methylthio)benzoic acid, N-(2-Furoyl)glycine, 2-(Methylthio)nicotinic acid, 3-Fluoro-4-methoxybenzoic acid, Tfa-Gly-OH, 2-Naphthoic acid, Quinaldic acid, Ac-L-Ile-OH, 3-Methylindene-2-carboxylic acid, 2-Quinoxalinecarboxylic acid, 1-Methylindole-2-carboxylic acid, 2,3,6-Trifluorobenzoic acid, N-Formyl-L-Met-OH, 2-[2-(2-Methoxyethoxy)ethoxy]acetic acid, 4-n-Butylbenzoic acid, N-Benzoylglycine, 5-Fluoroindole-2-carboxylic acid, 4-n-Propoxybenzoic acid, 4-Acetyl-3,5-dimethyl-2-pyrrolecarboxylic acid, 3,5-Dimethoxybenzoic acid, 2,6-Dimethoxynicotinic acid, Cyclohexanepentanoic acid, 2-Naphthylacetic acid, 4-(1H-Pyrrol-1-yl)benzoic acid, Indole-3-propionic acid, m-Trifluoromethylbenzoic acid, 5-Methoxyindole-2-carboxylic acid, 4-Pentylbenzoic acid, Bz-b-Ala-OH, 4-Diethylaminobenzoic acid, 4-n-Butoxybenzoic acid, 3-Methyl-5-CF₃-isoxazole-4-carboxylic acid, (3,4-Dimethoxyphenyl)acetic acid, 4-Biphenylcarboxylic acid, Pivaloyl-Pro-OH, Octanoyl-Gly-OH, (2-Naphthoxy)acetic acid, Indole-3-butryic acid, 4-(Trifluoromethyl)phenylacetic acid, 5-Methoxyindole-3-acetic acid, 4-(Trifluoromethoxy)benzoic acid, Ac-L-Phe-OH, 4-Pentyloxybenzoic acid, Z-Gly-OH, 4-Carboxy-N-(fur-2-ylmethyl)pyrrolidin-2-one, 3,4-Diethoxybenzoic acid, 2,4-Dimethyl-5-CO₂Et-pyrrole-3-carboxylic acid, N-(2-Fluorophenyl)succinamic acid, 3,4,5-Trimethoxybenzoic acid, N-Phenylanthranilic acid, 3-Phenoxybenzoic acid, Nonanoyl-Gly-OH, 2-Phenoxyypyridine-3-carboxylic acid, 2,5-Dimethyl-1-phenylpyrrole-3-carboxylic acid, trans-4-(Trifluoromethyl)cinnamic acid, (5-Methyl-2-phenyloxazol-4-yl)acetic acid, 4-(2-Cyclohexenoxy)benzoic acid, 5-Methoxy-2-methylindole-3-acetic acid, trans-4-Cotininecarboxylic acid, Bz-5-Aminovaleric acid, 4-Hexyloxybenzoic acid, N-(3-Methoxyphenyl)succinamic acid, Z-Sar-OH, 4-(3,4-Dimethoxyphenyl)butyric acid, Ac-o-Fluoro-DL-Phe-OH, N-(4-Fluorophenyl)glutamic acid, 4'-Ethyl-4-biphenylcarboxylic acid, 1,2,3,4-Tetrahydroacridinecarboxylic acid, 3-Phenoxyphenylacetic acid, N-(2,4-Difluorophenyl)succinamic acid, N-Decanoyl-Gly-OH, (+)-6-Methoxy-a-methyl-2-naphthaleneacetic acid, 3-(Trifluoromethoxy)cinnamic acid, N-Formyl-DL-Trp-OH, (R)-(+)-

a-Methoxy-a-(trifluoromethyl)phenylacetic acid, Bz-DL-Leu-OH, 4-(Trifluoromethoxy)phenoxyacetic acid, 4-Heptyloxybenzoic acid, 2,3,4-Trimethoxycinnamic acid, 2,6-Dimethoxybenzoyl-Gly-OH, 3-(3,4,5-Trimethoxyphenyl)propionic acid, 2,3,4,5,6-Pentafluorophenoxyacetic acid, N-(2,4-Difluorophenyl)glutamic acid, N-Undecanoyl-Gly-OH, 2-(4-Fluorobenzoyl)benzoic acid, 5-Trifluoromethoxyindole-2-carboxylic acid, N-(2,4-Difluorophenyl)diglycolamic acid, Ac-L-Trp-OH, Tfa-L-Phenylglycine-OH, 3-Iodobenzoic acid, 3-(4-n-Pentylbenzoyl)propionic acid, 2-Phenyl-4-quinolinecarboxylic acid, 4-Octyloxybenzoic acid, Bz-L-Met-OH, 3,4,5-Triethoxybenzoic acid, N-Lauroyl-Gly-OH, 3,5-Bis(trifluoromethyl)benzoic acid, Ac-5-Methyl-DL-Trp-OH, 2-Iodophenylacetic acid, 3-Iodo-4-methylbenzoic acid, 3-(4-n-Hexylbenzoyl)propionic acid, N-Hexanoyl-L-Phe-OH, 4-Nonyloxybenzoic acid, 4'-(Trifluoromethyl)-2-biphenylcarboxylic acid, Bz-L-Phe-OH, N-Tridecanoyl-Gly-OH, 3,5-Bis(trifluoromethyl)phenylacetic acid, 3-(4-n-Heptylbenzoyl)propionic acid, N-Hepytanoyl-L-Phe-OH, 4-Decyloxybenzoic acid, N-(α,α,α -trifluoro-m-tolyl)anthranilic acid, Niflumic acid, 4-(2-Hydroxyhexafluoroisopropyl)benzoic acid, N-Myristoyl-Gly-OH, 3-(4-n-Octylbenzoyl)propionic acid, N-Octanoyl-L-Phe-OH, 4-Undecyloxybenzoic acid, 3-(3,4,5-Trimethoxyphenyl)propionyl-Gly-OH, 8-Iodonaphthoic acid, N-Pentadecanoyl-Gly-OH, 4-Dodecyloxybenzoic acid, N-Palmitoyl-Gly-OH, and N-Stearoyl-Gly-OH.

34. A composition comprising a plurality of compounds of the formula:

T^{MS} -L-MOI

wherein,

T^{MS} is an organic group detectable by mass spectrometry, comprising carbon, at least one of hydrogen and fluoride, and optional atoms selected from oxygen, nitrogen, sulfur, phosphorus and iodine;

L is an organic group which allows a T^{MS} -containing moiety to be cleaved from the remainder of the compound, wherein the T^{MS} -containing moiety comprises a functional group which supports a single ionized charge state when the compound is subjected to mass spectrometry and is selected from tertiary amine, quaternary amine and organic acid;

MOI is a nucleic acid fragment wherein L is conjugated to the MOI at a location other than the 3' end of the MOI; and
wherein no two compounds have either the same T^{ms} or the same MOI.

35. A composition according to claim 34 wherein the plurality is greater than 2.

36. A composition according to claim 34 wherein the plurality is greater than 4.

37. A composition according to claim 34 wherein the nucleic acid fragment has a sequence complementary to a portion of a vector, wherein the fragment is capable of priming nucleotide synthesis.

38. A composition according to claim 34 wherein the T^{ms} groups of members of the plurality differ by at least 2 amu.

39. A composition according to claim 34 wherein the T^{ms} groups of members of the plurality differ by at least 4 amu.

40. A composition comprising water and a compound of the formula:



wherein,

T^{ms} is an organic group detectable by mass spectrometry, comprising carbon, at least one of hydrogen and fluoride, and optional atoms selected from oxygen, nitrogen, sulfur, phosphorus and iodine;

L is an organic group which allows a T^{ms}-containing moiety to be cleaved from the remainder of the compound, wherein the T^{ms}-containing moiety comprises a functional

group which supports a single ionized charge state when the compound is subjected to mass spectrometry and is selected from tertiary amine, quaternary amine and organic acid; and

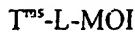
MOI is a nucleic acid fragment wherein L is conjugated to the MOI at a location other than the 3' end of the MOI; and

41. A composition according to claim 40 further comprising buffer, having a pH of about 5 to about 9.

42. A composition according to claim 40 further comprising an enzyme and one of dATP, dGTP, dCTP, and dTTP.

43. A composition according to claim 40 further comprising an enzyme and one of ddATP, ddGTP, ddCTP, and ddTTP.

44. A composition comprising a plurality of sets of compounds, each set of compounds having the formula:



wherein,

T^{ms} is an organic group detectable by mass spectrometry, comprising carbon, at least one of hydrogen and fluoride, and optional atoms selected from oxygen, nitrogen, sulfur, phosphorus and iodine;

L is an organic group which allows a T^{ms} -containing moiety to be cleaved from the remainder of the compound, wherein the T^{ms} -containing moiety comprises a functional group which supports a single ionized charge state when the compound is subjected to mass spectrometry and is selected from tertiary amine, quaternary amine and organic acid;

MOI is a nucleic acid fragment wherein L is conjugated to the MOI at a location other than the 3' end of the MOI;

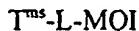
wherein within a set, all members have the same T^{ms} group, and the MOI fragments have variable lengths that terminate with the same dideoxynucleotide selected from ddAMP, ddGMP, ddCMP and ddTMP; and

wherein between sets, the T^{ms} groups differ by at least 2 amu.

45. A composition according to claim 44 wherein the plurality is at least 3.

46. A composition according to claim 44 wherein the plurality is at least 5.

47. A composition comprising a first plurality of sets of compounds according to claim 44, and a second plurality of sets of compounds having the formula



wherein,

T^{ms} is an organic group detectable by mass spectrometry, comprising carbon, at least one of hydrogen and fluoride, and optional atoms selected from oxygen, nitrogen, sulfur; phosphorus and iodine;

L is an organic group which allows a T^{ms}-containing moiety to be cleaved from the remainder of the compound, wherein the T^{ms}-containing moiety comprises a functional group which supports a single ionized charge state when the compound is subjected to mass spectrometry and is selected from tertiary amine, quaternary amine and organic acid;

MOI is a nucleic acid fragment wherein L is conjugated to the MOI at a location other than the 3' end of the MOI; and

wherein all members within the second plurality have an MOI sequence which terminates with the same dideoxynucleotide selected from ddAMP, ddGMP, ddCMP and, ddTMP; with the proviso that the dideoxynucleotide present in the compounds of the first plurality is not the same dideoxynucleotide present in the compounds of the second plurality.

48. A kit for DNA sequencing analysis comprising a plurality of container sets, each container set comprising at least five containers, wherein a first container contains a vector, a second, third, fourth and fifth containers contain compounds of the formula:



wherein,

T^{ms} is an organic group detectable by mass spectrometry, comprising carbon, at least one of hydrogen and fluoride, and optional atoms selected from oxygen, nitrogen, sulfur, phosphorus and iodine;

L is an organic group which allows a T^{ms}-containing moiety to be cleaved from the remainder of the compound, wherein the T^{ms}-containing moiety comprises a functional group which supports a single ionized charge state when the compound is subjected to mass spectrometry and is selected from tertiary amine, quaternary amine and organic acid; and

MOI is a nucleic acid fragment wherein L is conjugated to the MOI at a location other than the 3' end of the MOI; such that

the MOI for the second, third, fourth and fifth containers is identical and complementary to a portion of the vector within the set of containers, and the T^{ms} group within each container is different from the other T^{ms} groups in the kit.

49. A kit according to claim 48 wherein the plurality is at least 3.

50. A kit according to claim 48 wherein the plurality is at least 5.

51. A system for determining the sequence of a nucleic acid molecule in a sample, the sample including tagged nucleic acid fragments having nucleic acid fragments and tags attached to the nucleic acid fragments, comprising a separation apparatus that separates tagged nucleic acid fragments, a cleavage apparatus that receives separated tagged cleaves nucleic acid fragments and the tags from the nucleic acid fragments, each tag being correlative with a particular nucleotide of the nucleic acid fragment and detectable by electrochemical detection, and an apparatus for electrochemical detection that receives and detects electrochemical signatures of the tags.

52. A system according to claim 51 further including a data processor that correlates the electrochemical signature of a tag to a particular nucleotide and to a specific sample.

53. A system according to claim 51 wherein the apparatus for electrochemical detection is an apparatus for potentiostatic amperometry.

54. A system according to claim 52 wherein the data processor is capable of correlating the electrochemical signatures of five or more possible tags to a particular nucleotide and to five or more specific samples.

55. A system according to claim 52 wherein the data processor is capable of correlating the electrochemical signatures of sixteen or more possible tags to a particular nucleotide and to sixteen or more specific samples.

56. A system for determining the sequence of a nucleic acid molecule in a sample, the sample including tagged nucleic acid fragments having nucleic acid fragments and tags attached to the nucleic acid fragments, comprising a separation apparatus that separates tagged nucleic acid fragments, a cleavage apparatus that receives separated tagged nucleic acid fragments and cleaves from the nucleic acid fragments, each tag being correlative with a particular nucleotide of the nucleic acid fragment and detectable by mass spectrometry, a mass spectrometer that receives the tags and detects a mass of a tag, and a data processor that correlates the mass of a tag to a particular nucleotide and to a specific sample.

57. A system according to claim 56 wherein the data processor is capable of correlating the masses of five or more possible tags to a particular nucleotide and to five or more specific samples.

58. A system according to claim 56 wherein the data processor is capable of correlating the masses of sixteen or more possible tags to a particular nucleotide and to sixteen or more specific samples.